REMARKS

Claims 1-37 are pending and rejected.

CLAIM REJECTIONS UNDER 35 U.S.C. §§102 and 103

Applicant notes the Examiner's withdrawal of the rejection of claims 1-10, 13-29, and 31-33 under 35 U.S.C. §102(b) as anticipated by Boyce (Med. Biol. Eng. Comput. (1998) 36:791), and withdrawal of the rejection of claims 11-12 and 30 under 35 U.S.C. §103(a) as obvious over Boyce further in view of U.S. Patent No. 5,976,878.

However, applicant respectfully notes that the Examiner's statement of his basis for the withdrawal, as follows, does not contain the full substance of applicant's arguments. The Examiner states (emphasis in original):

> The cited art clearly teaches skin substitutes comprising cultured dermal cells on Collagen-GAG matrix, which further provides a lamination layer for cultured keratinocytes. However, the applicant argues that figure-1 of the prior art (**applicant's own publication**) does not anticipate the invention as claimed, since the prior art does not enable the claimed invention as there is no reasonable expectation of success of achieving the claimed invention without extensive and complex experimentation i.e., undue experimentation.

Applicant's arguments against these rejections were not so limited (pages 10-11, August 26, 2004 Preliminary Amendment filed with RCE). Applicant substantively distinguished and provided support for the claimed elements lacking in the reference, which renders the anticipation rejection improper, and by which the primary reference in the obviousness rejection fails. Specifically:

> As required, applicant states that the substance of the interview was the Office Action mailed June 16, 2004. Applicant, as author and inventor of the art of record, explained how his claimed invention is distinguished over his prior cited publication and cited patent, at least because the claimed invention requires dermal cells on the matrix, providing a lamination layer. Applicant clarified that the dermal cells were on an outer surface of the matrix, and has further amended the claims to reflect this. Applicant also explained how Figure 1 in his prior publication could neither anticipate his present invention, at least because Figure 1 does not enable the entire scope of the claimed invention as required for anticipation, nor could it render obvious his present invention, at least because there is no reasonable expectation of success of achieving the claimed invention without extensive and complex experimentation, as applicant explained, i.e., undue experimentation.

and

> Applicant respectfully reiterates his position that the pending claims are not anticipated because the claims require a dermal cellular layer on a biocompatible reticulated matrix, with the dermal cells providing a cellular lamination layer for cultured epidermal cells, as explained at least at page 20, lines 14-19:
>
> ...the fibroblasts or other dermal cells being inoculated need not fill these channels or openings in the matrix before the epidermal cells may be added. Rather, upon inoculation, the dermal cells attach to the reticulations, and thus are able to provide a continuous surface lamination...

CLAIM REJECTIONS UNDER 35 U.S.C. §112

Claims 1, 10, 18, 24, 28, 29, 32 and 34 are rejected under 35 U.S.C. §112 ¶1 as not described, and that the "outer surface of biocompatible reticulated matrix" is new matter. Applicant respectfully disagrees.

Applicant respectfully cites the following description in the originally filed application:

> Without being bound by a specific theory or mechanism, the following events likely occur. Upon inoculation, fibroblasts likely form a physiological attachment to the collagen matrix by binding via collagen-specific receptors. Because the matrix is reticulated and thus contains multiple continuous surfaces, as opposed to being perforated with direct channels or openings from a top surface to a bottom surface, the fibroblasts or other dermal cells being inoculated need not fill these channels or openings in the matrix before the epidermal cells may be added. Rather, upon inoculation, the dermal cells attach to the reticulations, and thus are able to provide a continuous surface lamination for the subsequently inoculation of epidermal cells within a shorter time period than is possible using a perforated matrix. (Page 20, lines 9-20, emphasis added.)

At least these portions of the specification clearly describe dermal cells on an outer surface of the biocompatible matrix, and therefore "outer surface of biocompatible reticulated matrix" is not new matter. Further, applicant respectfully asserts that one skilled in the art would know the outer surface of the biocompatible reticulated matrix based upon the teachings of the specification; the specification need not describe the claimed subject matter in exactly the same terms as used in the claims. *All Dental Prodx v. DMG Dental-Material* 64 USPQ2d 1945 (Fed. Cir. 2002); *In re Wertheim* 191 USPQ 90 (CCPA 1976).

Claims 1-37 are rejected under 35 U.S.C. §112 ¶1 as not enabled. Applicant respectfully disagrees.

As a preliminary matter, applicant notes that the amended claims, clarifying the position of dermal cells on an outer surface of the biocompatible matrix, were not previously rejected. Applicants have *infra* demonstrated support for these amendments in the originally filed specification.

Applicant emphatically disagrees with the Examiner regarding lack of enablement. Applicant's detailed description is in complete compliance with the requirement for "such particularity as to enable any person skilled in the pertinent art or science to make and use the invention without involving extensive experimentation." (MPEP §608.01(g)). It contains a full disclosure of the timing for device transplant (e.g., pages 7-8), properties of the engrafted device (e.g., page 8), sources for the cellular populations (e.g., pages 9-10), exemplary applications for the device (e.g., pages 10-11), preparation of the device (e.g., pages 11-12), still further detail of matrix preparation, including crosslinking (e.g., pages 12-15), cellular inoculation of the matrix, including descriptions of both submerged inoculation and lifted inoculation, as well as day-by-day steps (e.g., pages 15-20), description of cellular post-inoculation events (e.g., pages 20-21), preparation of the physiologic transplant site (e.g., page 21), surgical transplant procedures including vascularization, (e.g., page 21), and post-engraftment considerations including but not limited to graft beds, antimicrobial considerations, irrigation, dressings, etc. (e.g., page 21-22). These are detailed teachings, and not the "tossing out the mere germ of an idea", nor are they "vague intimations of general ideas that may or may not be workable" (Examiner's Office Action, page 6). Applicant also respectfully disagrees

with the Examiner that the application fails to disclose any skin device that is capable of engraftment in an animal and can be of any therapeutic use in a patient. If the Examiner's reference to a "workable" invention questions applicant's utility under 35 U.S.C. §101, applicant respectfully asserts that such a rejection has not been made and, moreover, it is established that data as required for an FDA submission is not required for patentability. *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995) and MPEP §2107. If the Examiner's reference to a "workable" invention questions applicant's disclosure, applicant respectfully asserts that he has fully complied with all requirements under this section. All processes were performed and are fully described in the detailed description, where there is no tense-specific language requirement. As analyzed above, applicant therefore respectfully but emphatically disagrees with the Examiner that "The examples provided in the specification as filed are prophetic and read as instructions rather than examples, leaving significant amount of experimentation necessary to practice the invention especially in view of applicants remarks filed on 08/26/04" (page 5).

As analyzed above, applicant also respectfully but emphatically disagrees with the Examiner's characterization

> the limited amount of guidance provided in the instant specification regarding the fate and functional effects of any other cell type in a bilayered skin construct...in the formation of artificial skin, it is highly unpredictable that such a combination would result in the formation of skin device [sic] that is capable of providing any engraftment benefits. (page 5).

Applicant respectfully but emphatically asserts that his detailed disclosure of specific and complete teachings for preparing, using, and evaluating the device, analyzed

above, meets the requirements under 35 U.S.C. §112, and thus disagrees that it is a "limited amount of guidance."

For at least these reasons, applicant respectfully requests these rejections be withdrawn.

CLAIM REJECTIONS UNDER 35 U.S.C. §102

Claims 1-7, 9-11, 13-15, 18-29, and 31-37 are rejected under 35 U.S.C. §102(b) as anticipated by Wilkins. Applicant respectfully disagrees.

Wilkins requires cultured human dermal fibroblasts (HDF) in a bovine type I collagen gel; its HDF had been combined with the polymer before polymerization. In other words, Wilkins requires cells in order to form its hydrated gel. HDF are combined with a neutralizing buffer/concentrated nutrient medium and a solution of bovine type I collagen, mixed uniformly at a specific density (~$3X10^4$ cells/mL), and poured into a layer of collagen to bond the cells onto a culture vessel (Figure 1). This results in HDF distributed through 75% of the thickness of a collagen gel, i.e., HDF in the matrix. The surface would have at most discontinuous isolated cells, and thus would not be a lamination layer.

In contrast, all of applicant's claims require a cellular lamination layer on the matrix. Simply put, applicant's cells are inoculated on an already-formed matrix. Applicant previously amended the claims to further clarify that "on" the matrix is on an outer surface of the matrix. Applicant reiterates his previous argument that the term "lamination" itself indicates a cover on the formed matrix

(laminate: to cover with thin sheets"). (The American Heritage Dictionary, Morris, Ed., Houghton Mifflin Company, Boston, 1976, p. 734 attached to this Amendment.)

For at least these reasons, applicant respectfully asserts the rejection is overcome and requests its withdrawal.

CLAIM REJECTIONS UNDER 35 U.S.C. §103

Claims 8, 12, 16-17 and 30 are rejected under 35 U.S.C. §103(a) as obvious of Wilkins in view of Boyce (Med. Biol. Eng. Comput. 36:791-800, 1998) and Boyce U.S. Patent No. 5,976,878. Applicant respectfully disagrees.

Each of claims 8, 12, 16-17, and 30 depends from a claim that requires a cellular lamination layer on a reticulated matrix. As previously distinguished, Wilkins does not disclose this, nor does Wilkins teach, suggest, or motivate a cellular lamination layer on a reticulated matrix. In fact, Wilkins teaches away from a cellular lamination layer on a reticulated matrix, because Wilkins requires mixing cells in with the polymer to form the matrix.

Because the primary reference fails, the secondary references cannot stand to render the invention obvious.

For at least these reasons, applicant respectfully asserts the rejection is overcome and requests its withdrawal.

CONCLUSION

In view of the Amendments, as well as the foregoing remarks, applicant respectfully submits that this application is in complete condition for allowance and requests reconsideration in this regard.

The Examiner is invited to telephone the applicant's undersigned representative with any questions. Moreover, applicant offers to conduct either a telephone or personal interview with the Examiner if the Examiner believes an interview would be helpful in order to facility prosecution.

Respectfully submitted,
WOOD, HERRON & EVANS, L.L.P.

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